

REMARKS

Claims 1-4, 6, 8-32, 34 and 36-55 are pending. Claims 1, 2, 4, 6, 8-16, 30-32, 34, 36-44 and 46-55 are under examination. Claims 1, 16, 30 and 31 have been amended. New claims 56-82 have been added. Support for the amendments and new claims can be found throughout the specification and the claims as filed. In particular, support for the amendment to claims 1, 16 and 30 can be found, for example, on page 22, lines 6-27, which indicates that a multidimensional coordinate point is defined by "n" parameters, where n is the number of molecules in a sample of molecules and each parameter is the level of expression of a molecule in the sample. Support for the amendment can also be found on page 3, line 21, to page 4, line 13, and Figures 1 and 2, which exemplify two-dimensional and three-dimensional space of n molecules, where n is two and three molecules, respectively; and on page 69, line 5, to page 72, line 8, which describes multidimensional space and exemplifies two-dimensional, three-dimensional and multidimensional coordinate points representative of the expression levels of n molecules in an individual. Support for new claims 56-82 can be found, for example, on page 51, lines 17-29. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested.

Applicants appreciate the time and helpful discussion with Examiner Marschel and Technical Specialist Woodward in the telephone interview conducted May 2, 2005, with the inventors, Dr. Hood and Dr. Siegel, and Applicants' representative. During the telephone interview, the rejection under 35 U.S.C. § 102 was discussed. The cited reference, Friend et al., U.S. Patent No. 6,218,122, was discussed as well as claim language believed by Applicants to distinguish the claims from Friend et al. Technical Specialist Woodward proposed a claim amendment that all agreed would further prosecution. Applicants believe that the response addresses the issues discussed during the telephone interview.

The rejection of claims 1, 2, 4, 6, 8-16, 30-32, 34, 36-44 and 46-55 under 35 U.S.C. § 102(a) and (e) as allegedly anticipated by Friend et al., U.S. Patent No. 6,218,122, is respectfully traversed. Applicants respectfully maintain, for the reasons of record, that the claims are novel over Friend et al.

Applicants maintain that Friend et al. does not teach the claimed methods. Claims 1, 16 and 30 have been amended to recite the step of creating a multidimensional space of n dimensions,

wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of individuals administered a drug or treated with a drug. As discussed in the telephone interview and the Rule 132 Declaration filed with the response mailed August 24, 2004, Friend et al. describes using unidimensional analysis, in contrast to the claimed invention that uses multidimensional analysis. As taught in the specification, a “multidimensional coordinate point” refers to a coordinate defined by “ n ” parameters, where n is the number of molecules in a sample of molecules and each parameter is the level of expression of a molecule in the sample (page 22, lines 6-10). The specification teaches exemplary multidimensional spaces containing multidimensional coordinate points in Figures 1 and 2. For example, Figure 1 shows a representative multidimensional space of two dimensions, where each circle represents a multidimensional coordinate point representative of the expression levels of two molecules in an individual (page 69, line 24, to page 70, line 2). Figure 2 shows a representative multidimensional space of three dimensions, where each circle represents a multidimensional coordinate point representative of the expression levels of three molecules in an individual (page 71, lines 7-15). The specification further teaches that similar analysis can be applied in n -dimensional space, where n is the number of molecules in a sample of molecules from an individual (page 71, lines 26-30).

The specification additionally teaches the distinction between “one-molecule-at-a-time” analysis, that is, unidimensional analysis, of multiple parameters and multidimensional analysis, as recited in the claims (page 69, lines 1-23). “Instead of comparing the expression levels of individual molecules of a sample to the corresponding health-associated reference expression intervals determined for a reference population, as in one-molecule-at-a-time analysis, the expression level of each molecule in the sample is compared to other molecules in the sample in a multidimensional analysis” (page 69, lines 8-14). Thus, the specification clearly teaches that one-molecule-at-a-time analysis, i.e., unidimensional analysis, is distinct from multidimensional analysis. Accordingly, Applicants respectfully submit that the claimed methods reciting “creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed,” “determining a multidimensional coordinate point” and “determining a drug response-associated reference expression region” are distinct from the unidimensional analysis described in Friend et al. As discussed in the Declaration filed with the previous response, the interpolated response curves of Friend et al. are unidimensional functions, meaning univariate functions, or functions of a single variable, and each such unidimensional function is for a single cellular constituent, i.e. molecule

(paragraph 4). Thus, Applicants respectfully maintain that the claimed methods using multidimensional analysis are distinct from the unidimensional analysis described in Friend et al.

With regard to the Declaration filed with the previous response, Applicants respectfully disagree with the assertions in the Office Action regarding the interpretation of Friend et al. described in the Declaration. Applicants respectfully submit that the Declaration submitted with the previous response provided the expert opinion of Dr. Hood and Dr. Siegel regarding unidimensional analysis described in Friend et al. and the distinctions of Friend et al. over the claimed methods directed to multidimensional analysis. As evidence of the expertise of Dr. Hood and Dr. Siegel, attached herewith as Exhibits A and B are their respective curricula vitae. Applicants respectfully submit that the Declaration filed with the previous response should be considered as corroborative evidence of the distinctions of the claimed methods over Friend et al. and respectfully request reconsideration of the Declaration in light of the telephone interview and the distinctions discussed above.

With regard to leukocyte specimens, Applicants wish to clarify the record. It appears in the Office Action that the previous response was interpreted to mean that Applicants argued that “white blood cells” and “leukocytes” are distinct. Applicants agree that “white blood cells” and “leukocytes” mean the same thing. In the previous response, however, it was noted that the only mention in Friend et al. of white blood cells or leukocytes is at column 12, lines 37-38.

In still other embodiments, perturbation response profiles are obtained for one or more disease states and/or for one or more drug therapies and are calibrated to a clinical effect or effects. Exemplary clinical effects include, but are not limited to, blood pressure, body temperature, blood or urine glucose levels, cholesterol levels (including, e.g., HDL and LDL levels) viral load levels, blood hematocrit levels, white cell count, tumor size etc. In fact, any measurement of a patient’s biochemical and/or physiological state that may be readily obtained in a clinical setting is a measurement of a clinical effect. (column 12, lines 31-41, emphasis added)

Friend et al. clearly describes using “white blood cell count,” i.e. leukocyte count, as one of the well known “clinical effects” routinely monitored by physicians to determine a patient’s “biochemical and/or physiological state.” However, Applicants respectfully maintain that Friend et al. does not teach using white blood cells or leukocytes as a specimen from an individual for determining the expression levels of molecules in the individual.

Accordingly, Applicants further maintain that the claims reciting using a leukocyte specimen are distinct from the description in Friend et al.

Applicants maintain that Friend et al. does not teach the claimed methods using multidimensional analysis. Absent such a teaching, Applicants respectfully maintain that the claims are novel over Friend et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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